12-Month disclosures of financial relationships with commercial interests:

<table>
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<th>Honorarium: Consultant</th>
<th>Honorarium: Advisory Board</th>
<th>Travel Expenses</th>
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<td>Travena</td>
<td>Jazz Pharmaceuticals</td>
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This presentation does not contain off-label or investigational use of drugs or products.
Planning Committee, Disclosures

- Vitaly Gordin, MD
  Director of Pain Division
  Penn State Hershey Medical Center
  Hershey, PA
  - No relevant financial relationships

- Jennifer Westlund, MSW
  Director of Education
  American Academy of Pain Medicine
  - No relevant financial relationships

- Angela Casey
  VP, Medical Director
  PharmaCom Group
  - No relevant financial relationships
Target Audience

- The overarching goal of PCSS-O is to offer evidence-based trainings on the safe & effective prescribing of opioid medications in the treatment of pain &/or opioid addiction.

- Our focus is to reach providers &/or providers-in-training from diverse healthcare professions including physicians, nurses, dentists, physician assistants, pharmacists, & program administrators.
Educational Objectives

• At the conclusion of this activity participants should be able to:
  1. Understand the major risk factors for unintentional opioid overdose deaths in patients with chronic pain
  2. Devise a plan to implement 8 simple principles for safer opioid prescribing that can save lives
Major Reasons for Opioid-Associated Deaths

• Over-prescribing (Physician)
  ▪ Starting dose too high
  ▪ Dose escalation too rapid
  ▪ Over reliance on conversion tables
  ▪ Inadequate risk assessment

• Non-adherence (Patient)
  ▪ To control pain
  ▪ To “cope”
  ▪ Substance abuse

• Unanticipated co-morbidities
  ▪ QT prolongation
  ▪ Pharmacogenetics & methadone metabolism
  ▪ Sleep disordered breathing
Rates of Prescription Opioid Sales & Deaths, 1999-2013

Sales per kg per 100,000 people
Deaths per 100,000 people

Number of Deaths Involving Opioid Analgesics, 1999-2013

4-fold increase in deaths since 1999

Prescription Opioid Deaths Are a Growing Problem Among Women

Although men are still more likely to die of prescription opioid overdoses, the gap between men & women is closing.

Eight Opioid Prescribing Principles for Providers

1. Assess patients for risk of abuse before starting opioid therapy and manage accordingly
2. Watch for and treat comorbid mental disease if present
3. Conventional conversion tables can cause harm and should be used cautiously when rotating (switching) from one opioid to another
4. Avoid combining benzodiazepines with opioids, especially during sleep hours
5. Start methadone at a very low dose and titrate slowly regardless of whether your patient is opioid tolerant or not
6. Assess for sleep apnea in patients on high daily doses of methadone or other opioids and in patients with a predisposition
7. Tell patients on long-term opioid therapy to reduce opioid dose during upper respiratory infections or asthmatic episodes
8. Avoid using long-acting opioid formulations for acute, post-operative, or trauma-related pain

Assess patients for risk of abuse before starting opioid therapy & manage accordingly

1

BEST PRACTICES

Oreos As Addictive As Cocaine? For Rats, At Least

Photo by Bob MacDonnell courtesy of Connecticut College

Vulnerability to Opioid Addiction

Individuals respond differently to opioid exposure.

Addictive disease after opioid exposure.

No addictive disease with exposure.

No addictive disease due to lack of exposure.
### Genetic Vulnerability to Addiction?

<table>
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<th></th>
<th>Fischer 344</th>
<th>Lewis Poly-substance Abuse</th>
<th>Sprague-Dawley Average</th>
<th>Drug neutral</th>
<th>Drug rejecting</th>
<th>Drug seeking</th>
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<td>Poly-substance Abuse</td>
<td>Average</td>
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Level of Abuse in Stressful Environments

Screening Tools to Assess Patient Risk Before Prescribing Opioids

- Use one of several available tools to assess patient risk of developing problematic drug-taking behaviors
  - Based on biological, social, & psychiatric risk factors

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<thead>
<tr>
<th>Tool</th>
<th># of items</th>
<th>Administered by</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORT Opioid Risk Tool</td>
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<td>patient</td>
</tr>
<tr>
<td>SOAPP® Screener &amp; Opioid Assessment for Patients with Pain</td>
<td>24, 14, or 5</td>
<td>patient</td>
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<tr>
<td>DIRE Diagnosis, Intractability, Risk, &amp; Efficacy Score</td>
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<td>clinician</td>
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- Implement a plan according to risk level
  - eg, for high-risk patients, refer for psychiatric evaluation or co-manage with a chemical dependency expert prior to opioid trial

Identify Misuse Once Opioid Treatment Begins

- Periodic monitoring for effects on analgesia, daily activities, adverse events, ADRBs, cognition, function, & QOL can be assisted by tools

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<td>COMM Current Opioid Misuse Measure</td>
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</table>

- Check state prescription monitoring programs
- Utilize measures such as urine drug testing

ADRBs=aberrant drug-related behaviors; QOL=quality of life

Watch for & treat comorbid mental disease if present

Overlapping Effects

Pain disorders

Psychiatric disorders

50% overlap

Overlapping Effects

60% overlap

Addiction disorders

Psychiatric disorders

Comorbid Pain & Mental Disease

- Co-occurrence of mental health disorders with chronic pain place patient at high risk for:
  - Misuse
  - Drug-drug interactions
  - Overdose
- Assess for the presence of mental disease before initiating opioid therapy
  - When indicated, consult with experts in mental health fields to co-ordinate care

An Olympian Challenge: Managing a Critical Interplay

A “trio diagnosis”

Addiction disorder
Psychiatric disorder
Pain disorder

Suicide

Number of ED visits for drug-related suicide attempts (thousands)

- **All drugs**
- **Opioid analgesics**

**41% increase in drug suicide attempts**

**87% increase in opioid suicide attempts**

Why Suicide? Non-Pain Patients

Escape from severe suffering

Only option

Hopelessness

Permanent solution

Conventional conversion tables can cause harm & should be used cautiously when rotating (switching) from one opioid to another.

Equianalgesic tables provide insufficient guidance to determine the equivalent doses of different opioids

- Individual consideration is necessary for every patient
Steps in Opioid Rotation

- Slowly decrease one opioid while slowly titrating the new opioid to effect
Steps in Opioid Rotation

- New drug: 10%-20% increments
- Old drug: 10%-30% increments
- IR Supplement: 10%-20% increments

Steps in Opioid Rotation

10%-20% increments
IR Supplement

New drug

10%-30% increments

Old drug

Steps in Opioid Rotation

- In most cases, the complete switch can occur within 3-4 weeks
- If you are not experienced in switching opioids in patients on long-term opioid therapy, seek expert consultation

Avoid combining benzodiazepines with opioids, especially during sleep hours.
Most Common Drugs Involved in Overdoses in the United States

- In 2013, there were 43,982 drug overdose deaths
  - 22,767 (51.8%) were related to pharmaceuticals
    - 16,235 (71.3%) involved opioid analgesics
    - 6,973 (30.6%) involved benzodiazepines
- People who died of drug overdoses often had a combination of benzodiazepines & opioids in their bodies
- In 2011, ~1.4 million ED visits involved nonmedical use of pharmaceuticals
  - 501,207 visits involved anti-anxiety & insomnia medications
  - 420,040 visits involved opioid analgesics

Benzodiazepines & Chronic Pain Patients

- Enhance the respiratory depressant effects of opioids
  - Frequently co-prescribed with opioids (up to 50% of patients)
    - In 1 population, 80% of patients prescribed high-dose opioids were co-prescribed benzodiazepines
    - More common in chronic pain patients with substance use disorders
- Consider an alternative
  - For anxiety disorders
  - When a sleep aid is indicated, eg, an anticonvulsant or low-dose trazodone
    - For patients with neuropathic pain, low-dose trazodone at bedtime may be dually beneficial

Start methadone at a very low dose & titrate slowly regardless of whether your patient is opioid tolerant or not.

Methadone-Related Deaths

- Methadone contributed to nearly 1 in 3 prescription opioid deaths in 2009

- 5,000 people die every year of overdose related to methadone

- 6 times as many people died of methadone overdose in 2009 than a decade before

CDC. Prescription Drug Overdoses. CDC Vital Signs; July 2012.
Death Rate from Overdose Caused by a Single Prescription Painkiller


Simulated Methadone Dosing

- α (analgesic)
- β (non-analgesic)

Blood level vs. Hours and Days

Toxicity

Analgesia
Legal Review of Opioid Deaths: Methadone

- Starting doses 20-140 mg/day
  - Most <30 mg/day
- ~90% opioid tolerant
- ~80% died within 4 days of first methadone
- Snoring common
- Occasional upper respiratory infection/flu onset preceded death

Initiating Methadone

- Consider starting patients, whether or not they are opioid naïve, on \( \leq 15 \text{ mg/day} \) in divided doses (qh8)
- Increase the total daily dose by no more than 25%-50%, no more frequently than weekly

If you are not experienced prescribing methadone, consult with a clinician who is

Assess for sleep apnea in patients on high daily doses of methadone or other opioids & in patients with a predisposition.

Sleep Disorders & Opioids: Events per Hour

Bars indicate hi/lo of 95% CI

- AHI ≥5 events/hour
- CAI ≥5 events/hour
- OMAI ≥5 events/hour
- Sleep apnea: type indeterminate

n = 140

AHI=apnea-hypopnea index
CAI=central apnea index
OMAI=obstructive & mixed apnea Index

Rate Ratios by Increase of Morphine Equivalent Dose

Assess for Sleep Apnea

- Refer the following patients for formal sleep apnea evaluation
  - Patients who require >50 mg/day of methadone
  - Patients who require >150 mg/day of morphine equivalent dose of other opioids
  - Patients with a predisposition or risk factors for sleep apnea
- At risk patients may require inpatient evaluation to monitor for & determine safety of opioid therapy

Tell patients on long-term opioid therapy to reduce opioid dose during upper respiratory infections or asthmatic episodes.
Reduce Opioid Dose During

- Because of a decreased margin of safety, advise patients to reduced their daily opioid doses by ≥30% during events with acute respiratory tract compromise
  - These include:
    - Flu
    - Pneumonia
    - Upper respiratory infections
    - Cigarette use
    - Chronic obstructive pulmonary disease
    - Asthmatic episodes

Avoid using long-acting opioid formulations for acute, post-operative, or trauma-related pain

Reserve Long-Acting Opioids for Opioid-Tolerant Patients

- Reserve long-acting/extended-release opioids, including transdermal patches, for patients who have developed tolerance to opioids
  - ie, who already take regular, daily, around-the-clock opioids
- Do not use for acute, postoperative, or trauma-related pain

• Paulozzi L. CDC. Populations at risk for opioid overdose. 2012.
• Student-faculty research suggests Oreos can be compared to drugs of abuse in lab rats. *Connecticut College News.* October 15, 2013.
• SAMHSA, Center for Behavioral Statistics and Quality, Drug Abuse Warning Network Medical Examiner Component, 2009.
• Webster LR. Unintentional overdose deaths: reversing the trend. Presented at: The American Academy of Pain Medicine 28th Annual Meeting; Feb 22-26, 2012; Palm Springs, CA.
Questions & Answers

Please type your question in the text chat box
PCSS-O Colleague Support Program

• PCSS-O Colleague Support Program is designed to offer general information to health professionals seeking guidance in their clinical practice in prescribing opioid medications.
• PCSS-O Mentors comprise a national network of trained providers with expertise in addiction medicine/psychiatry and pain management.
• Our mentoring approach allows every mentor/mentee relationship to be unique and catered to the specific needs of both parties.
• The mentoring program is available at no cost to providers.

For more information on requesting or becoming a mentor visit: pcss-o.org/ask-colleague

• Listserv: A resource that provides an “Expert of the Month” who will answer questions about educational content that has been presented through PCSS-O project. To join email: pcss-o@aaap.org.
PCSS-O is a collaborative effort led by American Academy of Addiction Psychiatry (AAAP) in partnership with: Addiction Technology Transfer Center (ATTC), American Academy of Neurology (AAN), American Academy of Pain Medicine (AAPM), American Academy of Pediatrics (AAP), American College of Physicians (ACP), American Dental Association (ADA), American Medical Association (AMA), American Osteopathic Academy of Addiction Medicine (AOAAM), American Psychiatric Association (APA), American Society for Pain Management Nursing (ASPMN), International Nurses Society on Addictions (IntNSA), and Southeast Consortium for Substance Abuse Training (SECSAT).

For more information visit: www.pcss-o.org
For questions email: pcss-o@aaap.org

Twitter: @PCSSProjects

Funding for this initiative was made possible (in part) by Providers’ Clinical Support System for Opioid Therapies (grant no. 1H79TI025595) from SAMHSA. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.